PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 14031-2	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/CA 03/01387	International filing date *(day/month/year)* 19.09.2003	Priority date *(day/month/year)* 19.09.2002
International Patent Classification (IPC) or both national classification and IPC A61K31/00		
Applicant UNIVERSITY HEALTH NETWORK et al		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 8 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☒ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
19.04.2004	05.11.2004
Name and mailing address of the international preliminary examining authority: European Patent Office - Gitschiner Str. 103 D-10958 Berlin Tel. +49 30 25901 - 0 Fax: +49 30 25901 - 840	Authorized Officer Beyss, E Telephone No. +49 30 25901-344

Form PCT/IPEA/409 (Cover Sheet) (January 2004)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/CA 03/01387

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-63 as originally filed

Sequence listings part of the description, Pages

1-12 as originally filed

Claims, Numbers

1-11 as originally filed

Drawings, Sheets

1-16 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application,

   ☒ claims Nos. 4, 5, 7, 8 with respect to industrial applicability

   because:

   ☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (specify):

   ☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

   ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

   ☒ no international search report has been established for the said claims Nos. 4, 5, 7, 8 with respect to industrial applicability

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the Standard.

   ☐ the computer readable form has not been furnished or does not comply with the Standard.

IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees, the applicant has:

   ☐ restricted the claims.

   ☐ paid additional fees.

   ☐ paid additional fees under protest.

   ☒ neither restricted nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

☐ complied with.

☐ not complied with for the following reasons:

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

☐ all parts.

☒ the parts relating to claims Nos. 1, 2, 4, 5, 7-11 .

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	
	No:	Claims	1, 2, 4, 5, 7-11
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1, 2, 4, 5, 7-11
Industrial applicability (IA)	Yes:	Claims	1, 2, 9-11
	No:	Claims	

2. Citations and explanations

see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claims 4, 5, 7, 8. relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Re Item IV

Lack of unity of invention

In respect of the present application, only part of the claimed subject-matter has been searched, following an objection of lack of unity of invention by the International Searching Authority (see Article 17 (3)(a) PCT).

As outlined in the International Search Report (ISR) the International Searching Authority (ISA) found multiple inventions in this international application, which were considered not to be linked by a single inventive concept in the sense of Rule 13.1 and 13.2 PCT. Therefore, the requirements of Article 17(3)(a) PCT were considered not to be fulfilled. The International Examination Authority (IEA) fully supports the non-unity objection of the ISA.

This Authority considers that there are 6 inventions covered by the claims indicated as follows:

Invention 1: claims 1, 2, 4, 5, 7-11 all in part
The use of an inactive PI3K gamma or an inactive fragment of PI3K gamma for the treatment of a heart disease

Invention 2: claims 1, 2, 4, 5, 7-11 all in part
The use of an antibody of PI3K gamma for the treatment of a heart disease

Invention 3: claims 1, 2, 4, 5, 7-11 all in part
The use of an antisense oligonucleotide that inhibits the expression of PI3K gamma for the treatment of a heart disease

Invention 4: claims 1, 3, 4, 6-11 all in part
The use of wortmannin for the treatment of a heart disease

Invention 5: claims 1, 3, 4, 6-11 all in part
The use of LY294002 for the treatment of a heart disease

Invention 6: claims 1, 3, 4, 6-11 all in part
The use of quercetin for the treatment of a heart disease

The reasons for which the inventions are not so linked as to form a single general inventive concept, as required by Rule 13.1 PCT, are as follows:
The problem underlying the application is a method for treating a heart disease.
The solution is the use of an inhibitor of PI3K gamma.

The ISA has found that this feature was known already in the prior art.

- WO-A-0003746 discloses the use of wortmannin for the treatment of a myocardial infarction (page 21, line 16; claims 1, 16, 17).

Due to the fact that the use of wortmannin for the treatment of heart diseases is already known and there are substantial structural differences between the claimed compounds and no other technical feature can be distinguished which, in the light of the prior art, could be regarded as special technical feature in the sense of Rule 13.2 PCT the ISA is of the opinion that there is no single inventive concept underlying the six claimed inventions of the present application in the sense of Rule 13.1 PCT.
Consequently there is a lack of unity and the different inventions, not belonging to a common inventive concept, are formulated as the different subjects on the communication pursuant to Art. 17(3)(a) PCT.

The Applicant has not paid additional search fees for inventions 2-6. The Applicant can now obtain a Written Opinion in respect of those parts of the application which have been searched namely the first invention based on claims 1, 2, 4, 5, 7-11.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

For the assessment of the present claims 4, 5, 7, 8 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Reference is made to the following document:

D1: WO-A-0003746

1. Novelty

D1 describes the use of wortmannin for the treatment of a myocardial infarction (claims 1, 16; page 21, line 16).

Invention 1 of present application discloses the use of an inactive PI3K gamma or an inactive fragment of PI3K gamma for the treatment of a heart disease. The subject-matter of claims 1, 2, 4, 5, 7-11 is therefore novel.

2. Inventive Step

D1 is considered to represent the most relevant state of the art. The problem to be solved by the present invention may therefore be regarded as the provision of a pharmaceutical composition for the treatment of a heart disease.

The solution proposed in claims 1, 2, 4, 5, 7-11 of the present application can be considered as involving an inventive step (Article 33(3) PCT) since D1 does not mention an inactive PI3k gamma nor gives a hint nor suggestion to use an inactive PI3K gamma or an inactive fragment of PI3K gamma for the treatment of a heart disease.

3. Clarity

3.1.
Present claims 1, 4, 9 relate to the use of an inhibitor of PI3K gamma. No further true technical characteristics of this compound is given, but rather a definition by reference to a result to be achieved is attempted rendering the scope of said claims unclear (Art. 6 PCT).

3.2.
Claims 10, 11 do not meet the requirements of Article 6 PCT in that the matter for which protection is sought is not clearly defined. The claims attempt to define the subject-matter in terms of the result to be achieved, which merely amounts to a statement of the underlying problem, without providing the technical features necessary for achieving this result.

4. Industrial Applicability

Claims 1, 2, 4, 5, 7-11 meet the requirements of Article 33(4) PCT.